REMARKS

Reconsideration of the present Application in view of the present Amendments and the following remarks is respectfully requested. Claims 1-98 are currently pending. Non-elected claims 1 and 15-98 and claims 2-5, 7, and 11 have been cancelled without acquiescence to any rejection and without prejudice to further prosecution of this subject matter in a related divisional, continuation, or continuation-in-part application. Claims 6, 10, 12, and 14 have been amended and new claims 99-104 have been added to define more clearly the subject matter encompassed by Applicants' invention. Support for the amended claims may be found in the specification, for example, at page 10, line 23 through page 11, line 19; and page 13, line 28 through page 14, line 13. The specification has been amended to correct the sequence identifying numbers for the nucleotide sequences depicted in Figures 1 and 4 and to correct typographical errors. No new matter has been added.

The enclosed electronic and paper copies of the Sequence Listing include no new matter that goes beyond the original application as filed. Furthermore, the above amendments, which merely direct the insertion of the Sequence Listing and insertion of sequence identifiers, include no matter that goes beyond the original application as filed. Applicants respectfully submit that the above-identified application is in compliance with 37 C.F.R. §§ 1.821-1.825 and WIPO Standard ST. 25.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)

The PTO rejects claims 2-14 under 35 U.S.C. § 112, first paragraph, asserting that the claims are directed to subject matter that is not adequately described in the specification. More specifically, the PTO asserts that a single representative human polynucleotide species (SEQ ID NO:1) encoding a dual specificity phosphatase-15 (DSP-15) polypeptide (SEQ ID NO:2) capable of dephosphorylating phosphotyrosine and phosphoserine/phosphothreonine residues is disclosed, and that the specification does not describe any particular structure to function relationship of the "claimed modified sequences or sequences of varying lengths."

Applicants respectfully traverse this rejection and submit that Applicants possessed the claimed invention, as disclosed in the present specification and recited in the

instant claims, at the time the Application was filed. Applicants submit that in view of the Amendments submitted herewith, which include cancellation of claims 2-5, 7, and 11, the rejection of these claims is rendered moot.

Applicants' invention is directed in pertinent part to an isolated polynucleotide that encodes a DSP-15 substrate trapping mutant polypeptide in which a DSP-15 polypeptide comprising an amino acid sequence set forth in SEQ ID NO:2 has a substitution of an amino acid residue that is selected from (i) the aspartic acid residue at position 382 of SEQ ID NO:2 and (ii) the cysteine residue at position 413 of SEQ ID NO:2, such that the DSP-15 substrate trapping mutant polypeptide retains the ability to bind a DSP-15 substrate, and such that the ability of the DSP-15 substrate trapping mutant polypeptide to dephosphorylate the DSP-15 substrate is reduced relative to that of a wildtype DSP-15 polypeptide. In a certain embodiment, the invention is related to an isolated polynucleotide that encodes a DSP-15 substrate trapping mutant polypeptide in which Asp382 or Cys413 is substituted as recited, and that has a sequence at least 90% identical to the nucleotide sequence set forth in SEQ ID NO:1.

The specification provides a detailed description of relevant and identifying characteristics of the claimed polynucleotides encoding a DSP-15 substrate trapping mutant polypeptide that reasonably conveys to a person skilled in the art that Applicants possessed the claimed invention. In particular, the specification describes the structure of the encoded DSP-15 substrate trapping mutant polypeptide and its function as related to the described structure. The specification describes by its precise structure a polynucleotide sequence SEQ ID NO:1 that encodes the polypeptide sequence set forth in SEQ ID NO:2, and also describes polynucleotide variants that encode the same or related polypeptides. A variant DSP-15 polynucleotide may contain one or more substitutions, additions, deletions, and/or insertions that do not affect the activity of the encoded polypeptide (*e.g.*, page 14, lines 1-13), for example, conservative amino acid substitutions (*e.g.*, page 11, line 20 through page 12, line 4) in non-critical regions that do not substantially change the activity of the DSP-15 polypeptide (*e.g.*, page 11, lines 12-24). Such a polynucleotide variant may exhibit, for example, at least 90% identity to a polynucleotide sequence (*e.g.*, SEQ ID NO:1) that encodes a native or wildtype DSP-15 (*e.g.*, page 14, lines 5-13).

A DSP-15 polypeptide variant that is a modified form of DSP-15 is a substrate trapping mutant polypeptide that has a specific function disabled (*see, e.g.,* specification, page 10, lines 23-28). According to the instant specification, a DSP-15 substrate trapping mutant polypeptide thus retains the ability to bind a substrate and to form a stable enzyme substrate complex, but displays a reduced ability to dephosphorylate a substrate (*see, e.g.,* page 11, lines 1-19). The specification describes a polynucleotide encoding a DSP-15 substrate trapping mutant that comprises a substitution in the codon for the aspartic acid at position 382 (Asp382) or a substitution in the codon for the cysteine residue at position 413 (Cys413) of SEQ ID NO:2 (*e.g.,* page 11, lines 10-13; *see also, e.g.,* page 16, lines 25-29). The specification also provides examples of amino acid residues that may be substituted for Asp382 or Cys413 of SEQ ID NO:2, for example, alanine for the aspartic acid residue and serine for the cysteine residue (*id.*). In addition to alanine, Asp382 may be replaced with any of a number of different amino acids, including valine, leucine, isoleucine, proline, phenylalanine, tryptophan, asparagine, glutamine, lysine, arginine, and histidine (*see, e.g.,* WO 98/04712, page 9, lines 9-18, which is incorporated by reference in its entirety into the present application (*see* specification, page 9, lines 7-10)). Substitution of Cys413 with serine is also provided as an illustration, not a limitation, and may be replaced with other amino acids, for example, alanine (*see, e.g.,* WO 98/04712, page 7, lines 29 through page 8, line 15). Thus, the Application discloses the correlation between the structure and the function of a DSP-15 substrate trapping mutant polypeptide encoded by the claimed polynucleotides.

Accordingly, Applicants respectfully submit that the claimed subject matter is sufficiently described by the specification to reasonably convey to a person skilled in the art that Applicants possessed the claimed invention at the time the Application was filed. Applicants therefore submit that the instant Application complies with the written description requirement under 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (ENABLEMENT)

The PTO rejects claims 2-14 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The PTO alleges that the specification does not enable a person skilled in the art,

without undue experimentation, to make and use polynucleotide fragments encoding a polypeptide that is 10 or 15 amino acids in length or to make and use a polynucleotide encoding a DSP-15 polypeptide having 50% identity to SEQ ID NO:2. The PTO asserts that the disclosure in the specification is not commensurate with the scope of the claims.

Applicants respectfully traverse this rejection and submit that as disclosed in the present specification and recited in the instant claims as amended herewith, Applicants fully enabled the claimed invention at the time the instant Application was filed. Applicants submit that in view of the present Amendments, which include cancellation of claims 2-5, 7, and 11, the rejection of these claims is rendered moot.

As noted above, Applicants' invention is directed in pertinent part to an isolated polynucleotide that encodes a DSP-15 substrate trapping mutant polypeptide in which a DSP-15 polypeptide comprising the amino acid sequence of SEQ ID NO:2 has a substitution of an amino acid residue at the aspartic acid residue at position 382 (Asp382) of SEQ ID NO:2 or the cysteine residue at position 413 (Cys413) of SEQ ID NO:2, such that the DSP-15 substrate trapping mutant polypeptide retains the ability to bind a DSP-15 substrate. The ability of such a DSP-15 substrate trapping mutant polypeptide to dephosphorylate the DSP-15 substrate is reduced relative to that of a wild-type (*i.e.*, non-mutant) DSP-15 polypeptide.

Applicants submit that the specification provides explicit guidance enabling a person skilled in the art to make and use the claimed polynucleotides encoding a DSP-15 substrate trapping mutant polypeptide readily and without undue experimentation. The present Application discloses wildtype DSP-15 coding (SEQ ID NO:1) and translated (SEQ ID NO:2) sequences and provides abundant support for making therefrom and using a polynucleotide encoding a DSP-15 substrate trapping mutant that comprises a substitution of the aspartic acid at position 382, or a substitution of the cysteine residue at position 413 of SEQ ID NO:2 (*e.g.*, page 11, lines 9-12). Substitution of either Asp382 or Cys413 of SEQ ID NO:2 to make a DSP-15 substrate trapping mutant may be accomplished by any one of numerous different techniques that are known in the art and disclosed in the specification (*e.g.*, page 11, lines 9-12; page 16, lines 25-29). The specification thus teaches how to make and use a modified form of a DSP-15 polypeptide that has a specific function disabled (*see also*, *e.g.*, page 10, lines 5-27).

The specification also teaches that a variant DSP-15 polypeptide may contain conservative amino acid substitutions (*e.g.*, page 11, line 20 through page 12, line 4) in non-critical regions that do not substantially change the activity of the DSP-15 polypeptide (*e.g.*, page 12, lines 5-16). Such a variant of the disclosed polynucleotide sequence may exhibit, for example, at least about 90% identity to a polynucleotide sequence that encodes a DSP-15 polypeptide (*e.g.*, SEQ ID NO:1; *see, e.g.*, page 14, lines 1-12).

Also provided by the specification in view of the state of the art are assays for detecting substrate binding by a DSP-15 substrate trapping mutant, and for determining whether the ability of the DSP-15 substrate trapping mutant polypeptide to dephosphorylate a DSP-15 substrate is reduced relative to the (non-mutant) DSP-15 polypeptide (*e.g.*, page 10, line 23 through page 11, line 19; page 21, line 16 through page 23, line 13, and publications cited therein). The DSP-15 substrate trapping mutant polypeptide may then be used, for example, to identify DSP-15 substrates (*e.g.*, page 10, lines 22-27). Applicants submit that given the teachings of the instant Application, undue experimentation would not be required to perform any of the aforementioned methods to make and use the claimed polynucleotides encoding a DSP-15 substrate trapping mutant polypeptide.

Applicants therefore submit that the disclosure of the specification enables a skilled artisan to make and use the claimed invention, and that the disclosure is commensurate with the scope of the claimed subject matter. Accordingly, Applicants respectfully submit that the present Application satisfies all requirements of 35 U.S.C. § 112, first paragraph, and request that the rejection be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The PTO rejects claims 6-9 and 14 under 35 U.S.C. § 112, second paragraph, for indefiniteness. In particular, the Action asserts that abbreviations such as "DSP-15" and "MAP" are unclear.

Applicants submit that in view of the Amendments to claim 6 (upon which claims 8 and 9 depend) and to claim 14, the basis for the rejection has been obviated. The amended claims define the abbreviation "DSP-15" as "dual specificity phosphatase-15 (DSP-15)" (*see*

specification, page 9, line 27 through page 10, line 3). Further, in view of the Amendments submitted herewith, none of the claims recites the abbreviation "MAP" or depends on a claim that recites this abbreviation; therefore, this basis for rejection of the claims has been obviated.

Accordingly, Applicants respectfully submit that the claims meet the requirements for definiteness under 35 U.S.C. § 112, second paragraph, and request that rejection of these claims be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 102

The PTO rejects claims 2-3 and 10 under 35 U.S.C. § 102(e), alleging that the subject matter of the claims is anticipated by Liou *et al.* (WO 02/20732). In particular, the PTO asserts that Liou et al. disclose a polynucleotide having two regions of approximately 323 and 480 contiguous nucleotides that are identical to regions of SEQ ID NO:1 and an overall percent identity of 35%. The PTO also rejects claims 2-3 and 10 for lack of novelty under 35 U.S.C. § 102(e), asserting the subject invention is anticipated by Tang et al. (WO 02/22660). Specifically, the PTO asserts that Tang et al. disclose a polynucleotide that has a sequence 100% identical to nucleotides 1-851 of SEQ ID NO:1 and an overall 43% shared sequence identity. Claims 2-3 and 10 also stand rejected under 35 U.S.C. § 102(a) for being anticipated by a polynucleotide disclosed in GenBank Accession No. BE531347, which allegedly has 710 consecutive nucleotides identical to a region of SEQ ID NO:1 and which is alleged further to exhibit 36% overall sequence identity.

Applicants respectfully traverse this rejection and submit that none of the cited documents can be regarded as novelty-destroying. In view of the Amendments submitted herewith, which include cancellation of claims 2 and 3, Applicants submit that the rejection of these claims is rendered moot.

Applicants submit that none of the three cited documents teaches or suggests all elements of the claimed invention. The documents each fail to teach or suggest an antisense polynucleotide that is complementary to a polynucleotide that encodes a DSP-15 substrate trapping mutant polypeptide in which a DSP-15 polypeptide comprising an amino acid sequence set forth in SEQ ID NO:2 has a substitution of the aspartic acid residue at position 382 of SEQ

ID NO:2 or the cysteine residue at position 413 of SEQ ID NO:2. Each document also lacks any teaching or suggestion that such a DSP-15 substrate trapping mutant polypeptide or any DSP-15 substrate trapping mutant polypeptide retains the ability to bind a DSP-15 substrate but has a reduced ability to dephosphorylate the DSP-15 substrate relative to the ability of the unsubstituted DSP-15 polypeptide. Each cited document further fails to teach or suggest an expression vector that comprises a polynucleotide that encodes a DSP-15 substrate trapping mutant polypeptide as recited, a host cell comprising such an expression vector, and a method for producing a DSP-15 substrate trapping mutant polypeptide.

Accordingly, Applicants respectfully submit that the claims meet the novelty requirements under 35 U.S.C. § 102 and request that these rejections be withdrawn.

Applicants respectfully submit that all claims in the Application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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Enclosures:

Sequence Listing (paper)
CRF of Sequence Listing
Declaration Regarding Sequence Listing
Second Supplemental IDS
Form PTO-1449 (1 pg.)
1 reference

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